

INTISARI

Latar Belakang: Diabetes melitus merupakan keadaan hiperglikemia yang dapat meningkatkan stres oksidatif sehingga terjadi disfungsi endotel. Hal ini ditandai dengan ketidakseimbangan ET-1 dan eNOS yang semakin lama dapat merusak ginjal. Kerusakan ginjal ini dapat ditandai dengan peningkatan serum kreatinin dan fibrosis interstisial. Asam klorogenat diketahui memiliki efek renoprotektif namun masih diperlukan penelitian lebih lanjut terkait pengaruhnya terhadap disfungsi endotel.

Tujuan: Mengkaji pengaruh asam klorogenat terhadap disfungsi endotel dengan memeriksa fibrosis interstisial, kadar kreatinin serum, ekspresi mRNA ppET-1, dan eNOS pada ginjal tikus model diabetes melitus tipe 1.

Metode: Tikus galur Wistar jantan berusia 2 bulan ($n=30$) dibagi menjadi 6 kelompok: kontrol ($n=5$), kelompok DM yang diinduksi streptozotocin 60 mg/kgBB selama 1,5 bulan (DM1,5, $n=5$) dan 2 bulan (DM2, $n=5$), serta kelompok model DM 1,5 bulan yang diberikan 3 dosis asam klorogenat berbeda selama 2 minggu, yaitu 12,5 mg/kgBB (CGA1, $n=5$), 25 mg/kgBB (CGA2, $n=4$), dan 50 mg/kgBB (CGA3, $n=6$). Lalu dilakukan pengambilan sampel darah untuk memeriksa kadar kreatinin serum sebagai penilaian fungsi ginjal. Kemudian tikus diterminasi dan diambil sampel ginjal untuk ekstraksi RNA. Ekspresi mRNA ppET-1 and eNOS diukur menggunakan Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Area fibrosis interstisial diukur dengan pewarnaan Sirius Red (SR).

Hasil: Kadar kreatinin serum kelompok DM1,5 lebih rendah dibandingkan kontrol namun DM2 lebih tinggi dibandingkan kontrol. Kelompok CGA1, CGA2, dan CGA3 memiliki kadar kreatinin serum yang lebih rendah daripada DM2 ($p > 0,05$). Area fibrosis interstisial dan ekspresi mRNA ppET-1 kelompok DM1,5 dan DM2 lebih tinggi daripada kelompok kontrol. DM2 lebih tinggi daripada kelompok CGA1, CGA2, dan CGA3 ($p > 0,05$). Ekspresi mRNA eNOS pada kelompok DM1,5 dan DM2 lebih tinggi daripada kelompok kontrol dan semakin tinggi di CGA1. Namun kemudian kelompok CGA2 dan CGA3 lebih memiliki ekspresi mRNA eNOS yang lebih rendah daripada CGA1 ($p > 0,05$).

Kesimpulan: Asam klorogenat memiliki potensi untuk mencegah progresivitas diabetes melitus yang ditandai dengan menurunnya kadar kreatinin serum dan fibrosis interstisial salah satunya dengan cara menurunkan ekspresi mRNA ppET-1 serta eNOS.

Kata Kunci: diabetes melitus, asam klorogenat, disfungsi endotel, kreatinin, fibrosis interstisial, ET-1, eNOS

ABSTRACT

Background: Diabetes mellitus is a state of hyperglycemia that elevates oxidative stress resulting in endothelial dysfunction. It is characterized by the imbalance of ET-1 and eNOS which can damage the kidneys over time. Damaged kidney can be identified by an increase in serum creatinine and interstitial fibrosis. Chlorogenic acid is known to have a renoprotective effect but further research is needed regarding its effect on endothelial dysfunction.

Purpose: The aim of this study is to determine the effect of chlorogenic acid on interstitial fibrosis, serum creatinine level, preproEndothelin-1, and eNOS mRNA expression in rats with type 1 diabetes mellitus.

Method: Two months old Wistar rats (n=30) were divided into six groups: control (n=5), DM group which were induced with streptozotocin 60 mg/kgBW for 1,5 months (DM1,5, n=5) and 2 months (DM2, n=5), also 1,5 months DM group which were given 3 different doses of chlorogenic acid for 2 weeks, 12,5 mg/kgBW (CGA1, n=5), 25 mg/kgBW (CGA2, n=4), and 50 mg/kgBW (CGA3, n=6). Blood samples were taken for measuring serum creatinine level to assess kidney function. The rats were terminated and kidneys were harvested for RNA extraction and paraffin blocks preparation. The mRNA expression of ppET-1 and eNOS were measured using Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). The interstitial fibrosis area was measured by Sirius Red (SR) staining.

Result: Serum creatinine level in DM1,5 group was lower than the control group but DM2 was higher than the control. CGA1, CGA2, and CGA3 groups had lower serum creatinine level than DM2 ($p > 0,05$). Interstitial fibrosis area and ppET-1 mRNA expression in DM1,5 and DM2 were higher than those in the control group. DM2 was higher than the CGA1, CGA2, and CGA3 groups ($p > 0,05$). The expression of eNOS mRNA in the DM1,5 and DM2 groups was higher than control group, then went higher in the CGA1 group. But then CGA2 and CGA3 groups had lower eNOS mRNA expression than CGA1 ($p > 0,05$).

Conclusion: Chlorogenic acid may attenuate the progression of diabetes mellitus which marked by a decrease in serum creatinine level and interstitial fibrosis, by reducing the mRNA expression of ppET-1 and eNOS.

Keywords: diabetes mellitus, chlorogenic acid, endothelial dysfunction, creatinine, interstitial fibrosis, ET-1, eNOS